REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

Claims 1-3 and 5-51 are now in this application. Claim 4 is canceled, without prejudice or disclaimer, Claims 1, 5 and 6 are amended and Claims 27-51 are added. Claims 2, 3 and 7-26 remain as originally filed.

The Examiner's acknowledgment of applicant's Information Disclosure Statements and return of the Examiner-initialed copy of applicant's Forms PTO-1449 are noted, with appreciation. Applicant has received initialed copies of Sheets 1, 3, 4 and 5 of the five-sheet Form PTO-1449 filed January 17, 2002 and Sheet 1 of 1 of the Form PTO-1449 filed May 8, 2002. It is requested that an initialed copy of Sheet 2 of the Form PTO-1449 filed January 17, 2002, be provided with the next official communication.

The present application claims benefit of U.S. Provisional Application No. 60/224,358, filed August 11, 2000. See paragraph [0001] of the specification. It is requested that the Examiner acknowledge this claim for domestic priority under 35 U.S.C. § 119(e) in the next official communication.

Claims 1-26 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to be supported by the specification insofar as concerns the prevention of retinopathy. It is submitted that all of the claims now in the application are free of this rejection because the

words "prevent" and "prevention" no longer appear in the claims. Withdrawal of the rejection is in order.

Despite the foregoing, applicant notes that the Examiner seems to require that these terms be interpreted only in an absolute sense, meaning that the drug keeps the condition from happening forever. This was not applicant's intention. It is clear from the clinical data in the specification that a representative carbonic anhydrase inhibitor does indeed slow the progression of diabetic retinopathy such that, at the end of a two year test period, there was no overall change in the condition of the patients treated in accord with the invention. This included the situation in which diabetics who did not have retinopathy at the beginning of the test did not develop retinopathy during the two year treatment period, as well as the situation in which the condition of diabetics with early retinopathy had not worsened by the end of the two year period. In contrast, there was much more progression of retinopathy in the control group.

Since the Examiner does not consider the clinical data in the specification as supporting use of the term "prevention", the term "treatment" must be interpreted to include what applicant has shown, that is, that one can slow the progression of the disease to the extent that a diabetic not yet suffering from retinopathy does not even develop the condition during a two year treatment period. Apparently, to be entitled to use of the term "prevention", applicant would be required by the Examiner to show that the patients never developed retinopathy during their lifetimes! That was not applicant's understanding of

"prevention" as originally used in the claims, but rather that "prevention" meant that for a period of time a diabetic does not develop retinopathy when treated with a carbonic anhydrase inhibitor in accord with the invention. Since this apparently isn't considered "prevention" by the Patent and Trademark Office, it must be considered treatment, even when the condition has not yet developed in the diabetic at the time administration begins. Applicant thus does not consider deletion of "prevention" as narrowing the intended scope of his claims to the point of excluding what he has in fact shown by data in his specification. Claim 6 has been reworded accordingly.

Before discussing the art-based rejections, applicant would like to discuss the amendments to the claims set forth hereinabove, aside from amendments in response to the § 112, first paragraph, rejection already discussed.

Specifically, Claim 1 has been amended to exclude retinopathy associated with macular edema, i.e. the mammal in need of treatment for retinopathy does not have macular edema, and Claim 4 has accordingly been canceled. It is known that macular edema is associated with later stages of diabetic retinopathy, but macular edema does not occur during the early stages of diabetic retinopathy. All of Claims 1-3 and 5-26 now exclude treatment of patients with macular edema. As the original specification clearly discloses retinopathies that are not associated with macular edema as well as those which are, applicant is not introducing new matter by placing this limitation in his claims. Claims 27-51 also exclude treatment of mammals with macular edema; however, these claims also

specify that the carbonic anhydrase inhibitor is the sole active agent administered to treat retinopathy. Again, the specification clearly discloses this embodiment of the invention, so applicant is not adding new matter by placing such a limitation in the claims.

We turn now to the art-based rejections made by the Examiner.

Claims 1-15, 18 and 24-26 have been rejected under 35 U.S.C. § 102(b) as anticipated by Doshi et al. U.S. Patent No. 5,948,801 because Doshi et al. purportedly teach the use of the claimed carbonic anhydrase inhibitors for the treatment of the claimed conditions. Further, Claims 21-23 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Doshi et al. in view of applicant's admission that certain carbonic anhydrase inhibitors are known. Applicant submits that all of the claims now in this application are free of these rejections.

In making the 102 rejection, the Examiner refers to page 3, paragraphs 10, 12 and 13. The Doshi et al. patent has no page 3 and no paragraph numbers. If the Examiner is referring to page 3, paragraphs 10, 12 and 13 of the present application, applicant would point out that it is the claims of his application which must be considered vis-à-vis the cited patent. The cited Doshi et al. patent teaches the use of brinzolamide to treat retinal edema. In their statement of the background of the invention (column 1, lines 6-27), Doshi et al. emphasize the effect of carbonic anhydrase inhibition on the retinal pigment epithelium active secretion or pumping and cite the references for this point relating to other carbonic anhydrase inhibitors. Carbonic anhydrase inhibitors such as acetazolamide had previously

been thought to reduce macular edema in a variety of eye diseases. Doshi et al. appear to have patented a method for treating this edema with a new topical carbonic anhydrase inhibitor, brinzolamide, a method known to be useful of other members of that class of drugs. Doshi et al. list diabetic retinopathy and ischemic retinopathies as possible causes of macular edema, among others. Nowhere do they suggest that brinzolamide or other carbonic anhydrase inhibitors might be used for the treatment of these retinopathies in general. Doshi et al. limit their patent to the treatment of macular edema and not the treatment of the retinopathies that precede or lead to macular edema in some cases. It should be pointed out that, in general, only 10% of diabetics have diabetic macular edema whereas 50% or more have diabetic retinopathy. At the most, 25% of diabetics can expect to develop diabetic macular edema in their lifetime, whereas 60-90% of them can expect to develop retinopathy in their lifetime. The present patent provides treatment of diabetic retinopathy and other ischemic retinopathies and there are numerous features of these retinopathies, including microaneurysms, hemorrhages and neovascularization, which are not inclusive of diabetic macular edema. In contrast, Doshi et al. focus only on macular edema as such, which may have many different causes, only one of which is diabetic retinopathy. Moreover, Doshi et al. make no disclosure relevant to treatment of conditions which exclude macular edema, such as the early states of diabetic retinopathy. The instant specification presents clinical data showing that a carbonic anhydrase inhibitor (CAI) slows the progression of diabetic retinopathy such that no patients who were in the CAI group,

most of whom were in stage 1 (no retinopathy) or stage 2 (nonproliferative retinopathy) at the beginning of the test period, showed any overall progression of the disease by the end of the two year test period. These stage 1 and stage 2 patients did not have macular edema at the start of the test, nor did they develop macular edema during the two year test period. In contrast, there was more progression of retinopathy in the control group.

It is apparent from the foregoing that the Doshi et al. patent does not anticipate or render obvious any of applicant's claims, for applicant treats conditions which exclude the condition that Doshi et al. treat. Withdrawal of the 35 U.S.C. § 102(b) and 103(a) rejection is in order and is earnestly solicited.

Claims 16, 17 and 19 have been rejected under 35 U.S.C. § 102(b) as anticipated by WO 99/44603 because the WO document purportedly teaches use of the claimed carbonic anhydrase inhibitors for the treatment of the claimed disorders (page 2, lines 1-10; page 6, lines 20-23 and page 9, lines 10-14). Applicant submits that all of the claims now in the application are free of this rejection.

WO 99/44603 (hereafter referred to as "Sponsel") is directed to a method for treating macular disorders which comprises administering a carbonic anhydrase inhibitor combined with an ocular hypotensive agent. Sponsel's patent is not directed to treatment of diabetic retinopathy or other ischemic retinopathies. While he lists diabetic retinopathy and branch retinal vein occlusion as well as other causes of macular edema, he focuses solely on macular disorders. Nowhere does he suggest that carbonic anhydrase inhibitors

could be used to treat retinopathies in general or those not characterized by macular edema or deal with any other aspects of diabetic retinopathy such as microaneurysms, bleeding, neovascularization and so forth, only macular edema. Sponsel focuses on macular edema and macular degeneration and proposes short term treatment to improve vision. Sponsel's clinical Example 1 specifically excluded subjects with a history of any systemic disease such as diabetics. Indeed, none of his clinical examples have anything to do with diabetes. Applicant has provided the details of clinical studies showing his method effective in slowing the progress of diabetic retinopathy before the patients develop macular edema, and all of his claims are now exclusively drawn to the treatment of patients who do not have macular edema. There is not a scintilla of a suggestion by Sponsel of administering carbonic anhydrase inhibitors for the instantly claimed purpose. Moreover, new Claims 27-51 further distinguish from Sponsel. Sponsel requires a combination of a carbonic anhydrase inhibitor and an ocular hypotensive agent, while instant Claims 27-51 specify that the carbonic anhydrase inhibitor is the sole active agent administered to treat retinopathy.

Clearly, the claims now in this application are neither anticipated nor rendered obvious by Sponsel. Withdrawal of the record rejection is believed to be in order and is earnestly solicited.

In view of the foregoing, it is submitted that all record rejections have been overcome. Further favorable action in the form of a Notice of Allowance is believed to be next in order and is earnestly solicited.

Respectfully submitted,

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